L9 ANSWER 1 OF 4 MEDLINE
AN 2001492805 MEDLINE
DN 21426462 PubMed ID: 11535414
TI Bispecific and bifunctional single chain recombinant antibodies.
AU Kriangkum J; Xu B; Nagata L P; Fulton R E; Suresh M R
CS Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada T6G 2N8.
SO BIOMOLECULAR ENGINEERING, (2001 Sep) 18 (2) 31-40. Ref: 75
Journal code: 100928062. ISSN: 1389-0344.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20010906
Last Updated on STN: 20020122
Entered Medline: 20011207
AB Bispecific and bifunctional monoclonal antibodies as second generation monoclonals, produced by conventional chemical or somatic methods, have proved useful in the immunodiagnosis and immunotherapy of cancer and other diseases. **Recombinant antibodies produced** by genetic engineering techniques have also become available for use in preclinical and clinical studies. Furthermore, through genetic engineering, it is possible to remove or add on key protein domains in order to create designer antibody molecules with two or more desired functions. This **review** summarizes the strategies for development of single chain variable fragment (scFv) bifunctional and bispecific antibodies. The advantages and disadvantages as well as the problems of generating the various bispecific and bifunctional antibody constructs are reported and discussed. Since conventionally prepared bispecific and bifunctional monoclonal antibodies have already shown promise in clinical trials and results from preclinical studies of recombinant bispecific antibodies are encouraging, clinical trials in humans of recombinant bispecific and bifunctional antibodies, as a new generation of biologicals, are likely to be the thrust in the next decade and beyond.

L9 ANSWER 2 OF 4 MEDLINE
AN 2000115636 MEDLINE
DN 20115636 PubMed ID: 10648934
TI Transgenic milk as a method for the **production** of **recombinant antibodies**.
AU Pollock D P; Kutzko J P; Birck-Wilson E; Williams J L; Echelard Y; Meade H M
CS Genzyme Transgenics, One Mountain Rd, Framingham, MA 01701-9322, USA.
SO JOURNAL OF IMMUNOLOGICAL METHODS, (1999 Dec 10) 231 (1-2) 147-57. Ref: 60
Journal code: IFE; 1305440. ISSN: 0022-1759.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200002

ED Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000228

AB Recombinant antibodies and their derivatives are increasingly being used as therapeutic agents. Clinical applications of antibodies often require large amounts of highly purified molecules, sometimes for multiple treatments. The development of very efficient expression systems is essential to the full exploitation of the antibody technology. Production of recombinant protein in the milk of transgenic dairy animals is currently being tested as an alternative to plasma fractionation for the manufacture of a number of blood factors (human antithrombin, human alpha-1-antitrypsin, human serum albumin, factor IX). The ability to routinely yield mg/ml levels of antibodies and the scale-up flexibility make transgenic production an attractive alternative to mammalian cell culture as a source of large quantities of biotherapeutics. The following **review** examines the potential of transgenic expression for the **production** of **recombinant** therapeutic **antibodies**
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L9 ANSWER 4 OF 4 MEDLINE
AN 96231282 MEDLINE
DN 96231282 PubMed ID: 8699826
TI Recombinant antibodies: alternative strategies for developing and manipulating murine-derived monoclonal antibodies.
AU Peterson N C
CS Division of Immunology, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.
NC K01-RR-00103-01 (NCRR)
SO LABORATORY ANIMAL SCIENCE, (1996 Feb) 46 (1) 8-14. Ref: 69
Journal code: KYS; 1266503. ISSN: 0023-6764.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199609
ED Entered STN: 19960912
Last Updated on STN: 19960912
Entered Medline: 19960905

AB Since the introduction of hybridoma technology 20 years ago, numerous monoclonal antibodies with specificity to cellular, bacterial, and viral proteins have been developed. Application of monoclonal antibodies in biomedical research has substantially contributed to our understanding of the structural and physiologic components of intra- and extracellular protein interactions. Monoclonal antibodies that target antigens specific to infective agents or tumor cells may also be used as therapeutic agents.

Despite the versatility of these molecules, monoclonal antibody/hybridoma production is labor-intensive and requires the use of live animals. The fact that monoclonal antibodies are derived from animals limits their use as systemic therapeutic agents in humans. This can be attributed to the human anti-mouse antibody response that is mounted against these therapeutically administered foreign proteins. Recent advances in our understanding of immunoglobulin structure through three-dimensional studies--using nuclear magnetic resonance and X-ray crystallography and increased computer-assisted molecular modeling capabilities, combined with

the application of recombinant approaches--has led to the evolution of a new class of antibody-like molecules or man-made antibodies. The potential

of recombinant antibodies has been realized globally by academic and industrial institutions; the efficacy, toxicity, and pharmacokinetics of these antibody-derived compounds are being tested in a variety of animal models. This **review** summarizes various approaches for **producing recombinant antibodies** and discusses their potential as anti-cancer compounds so that those who are involved in relevant experimental animal protocols may gain a better understanding of this rapidly growing area. Additionally, by mimicking the affinity maturation of antibodies in vitro, phage display strategies have the potential to reduce or eliminate the use of animals in antibody production protocols.

L15 ANSWER 5 OF 5 MEDLINE
AN 92178225 MEDLINE
DN 92178225 PubMed ID: 1542295
TI Mechanism of allergic cross-reactions--III. cDNA cloning and variable-region sequence analysis of two IgE antibodies specific for trinitrophenyl.
AU Kofler H; Schnegg I; Geley S; Helmberg A; Varga J M; Kofler R
CS Department of Dermatology, University of Innsbruck, Austria.
SO MOLECULAR IMMUNOLOGY, (1992 Feb) 29 (2) 161-6.
Journal code: NG1; 7905289. ISSN: 0161-5890.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199204
ED Entered STN: 19920424
Last Updated on STN: 19920424
Entered Medline: 19920409
AB As a first step toward defining the molecular interactions between ligands and the IgE antigen-combining site, we report here the cDNA cloning and variable (V) region **nucleic acid** sequences of the heavy (H) and **light** (L) **chains** of 2 monoclonal mouse IgE **antibodies** to trinitrophenyl (ATCC-TIB142 = IGELa2 and ATCC-TIB141 = IGELb4). In all instances, full-length cDNA clones were obtained to facilitate future expression studies. The H chains were encoded by VH genes from the VH3660 and J558 gene families in context with DQ52 and DSP2.2 diversity (D) mini genes, and JH3 and JH4 joining (J) gene segments, respectively. Vk8/Jk2 and Vk1/Jk5 rearrangements encoded the respective L chain V-regions. Both antibodies exhibited considerable conservation of complementarity determining region (CDR) sequences, which will facilitate template-based computer modeling of the three-dimensional structures of complexes formed between various ligands and these antibodies. From sequence comparison between the dinitrophenyl (DNP)-binding myeloma protein MOPC-315 and these IgE antibodies likely candidates for hapten-contact residues within the binding sites of IGELa2 and IGELb4 have been suggested.

L15 ANSWER 1 OF 5 MEDLINE
AN 1998335922 MEDLINE
DN 98335922 PubMed ID: 9672201
TI Multifunctional g3p-peptide tag for current phage display systems.
AU Beckmann C; Haase B; Timmis K N; Tesar M
CS Division of Microbiology, GBF-National Research Centre for Biotechnology, Braunschweig, Germany.
SO JOURNAL OF IMMUNOLOGICAL METHODS, (1998 Mar 15) 212 (2) 131-8.
Journal code: IFE; 1305440. ISSN: 0022-1759.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19990129
Entered Medline: 19980803
AB We have previously described a monoclonal antibody (mAb), 10C3, directed against the gene-3 protein (g3p) of filamentous phage M13, which was produced to study g3p fusion protein expression in Escherichia coli and its incorporation in the phage capsid [Tesar, M., Beckmann, C., Rottgen, P., Haase, B., Faude, U., Timmis, K., 1995. Monoclonal antibody against pIII of filamentous phage: an immunological tool to study pIII fusion protein expression in phage display systems. Immunology 1, 53-54]. In this study we report mapping of the antigenic epitope of the mAb 10C3, by means of short overlapping peptide-sequences [Frank, R., Overwin, H., 1996. Spot synthesis. In: Morris, G.E. (Ed.), Methods in Molecular Biology, Vol. 66: Epitope Mapping Protocols. Humana Press, Totowa, NJ, pp. 149-169.] comprising the C-terminal half of the g3-protein. A minimal recognizable peptide was found which is represented in the 11 amino acid sequence from positions 292 to 302 of g3p [Wezenbeek van, P.M.G.P., Hulsebos, T.J.M., Schoenmakers, J.G.G., 1980. Nucleotide sequence of the filamentous bacteriophage M13 DNA genome: comparison with phage fd. Gene 11, 129-148].
In order to use the antibody also for detection and purification of recombinant proteins, such as single chain antibodies, the epitope was introduced as a tag sequence into the phagemid pHEN1 [Hoogenboom, H.R., Griffith, A.D., Johnson, K., Chiswell, D.J., Hudson, P., Winter, G., 1991. Multi-subunit proteins on the surface of the filamentous phage: methodologies for displaying **antibody** (Fab) **heavy** and **light chains**. **Nucleic Acid** Res. 19, 4133-4137; Nissim, A., Hoogenboom, H.R., Tomlinson, I.M., Flynn, G., Midgley, C., Lane, D., Winter, G., 1994. Antibody fragments from a single pot phage display library as immunochemical reagents. EMBO J. 13 (3) 692-698]. Purified single chain antibodies containing this tag were detectable down to a concentration of 2 ng ml(-1) under non-denaturing conditions (ELISA) or 4 ng per lane on immunoblots. The high sensitivity of the antibody for the peptide tag was reflected in the antibody affinity constant K(D) of 6.80 x 10(-10) M, which was determined by real time biomolecular interaction analysis (BIA) based on surface plasmon resonance (SPR) [Karlsson, R., Falt, A., 1997. Experimental design for kinetic analysis of protein-protein interactions with surface plasmon resonance biosensors. J. Immunol. Methods 200, 121-133]. Finally, recombinant proteins in E. coli periplasmic extracts could be purified in a single

step by affinity purification using immobilized mAb 10C3. These studies demonstrated that the new peptide-tag and its corresponding mAb represents a versatile tool for the detection of recombinant proteins selected by phage display technology.